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A hand-held probe for the biopsy and treatment of prostate cancer is being developed in a 30 month program. The probe is designed to acquire Magnetic Resonance Images and incorporates MR tracking coils for real-time localization during biopsy. Seven tasks were proposed for the execution of this project, three of which were scheduled for completion by the end of year one. Task 3 was eliminated in the final contract negotiations and is no longer scheduled for completion. The first and second tasks, however, have been completed. In the first task, changes were made to the MR tracking software, making it more suitable for dynamic prostate imaging. In the second task, "mock-ups" of several probes were made and evaluated in a cadaver model. The most promising design was then used to create a working prototype probe that includes MR tracking coils, an MR imaging coil and a biopsy channel. The performance of this probe was evaluated and compared to commercially available MR prostate imaging coils. The prototype probe was found to give a greater depth-of-penetration and twice the signal-to-noise ratio of the commercially available probe. The project is on schedule and no problems are anticipated in meeting the second year objectives.

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Introduction

A hand-held probe for the biopsy and treatment of prostate cancer is being developed in a 30 month program. The probe is designed to acquire Magnetic Resonance (MR) images, and incorporates MR tracking coils for real-time localization during biopsy procedures. Once the probe is properly placed, it can be used to insert a biopsy needle in the prostate to remove a tissue sample (or place therapeutic devices to destroy selected portions of the gland). Since the MR scanner employs a scan plane that is defined by the MR tracking coils within the probe, the images used for biopsy guidance are always registered to the path of the biopsy needle. Magnetic resonance imaging provides a much better view of the prostate gland (both normal and abnormal tissue) than is possible with any other imaging modality, including ultrasound. It is believed that this improved visualization of the prostate during biopsy will increase the specificity and reliability of the diagnosis and staging of prostate cancer. The scope of the research reported here includes the design, construction and evaluation of the MR biopsy probe. Evaluation of imaging aspects of the probe will be performed in human volunteers during the second year of the project. Evaluation of the biopsy capabilities of the probe will be performed in canine models in the last six months of the project.

Body

Progress – Year 1

Seven tasks were initially proposed in a 30 month program to develop an MR biopsy probe for the prostate. These tasks are shown in Figure 1 of this report (reproduced from Figure 6 of the proposal) and in greater detail in table 1. During contract negotiations, task 3 was eliminated to reduce the size of the contract.

Of the remaining six tasks, only the first two are scheduled to be performed in the first year of the project. Work on these tasks has proceeded on schedule and is described in detail below.

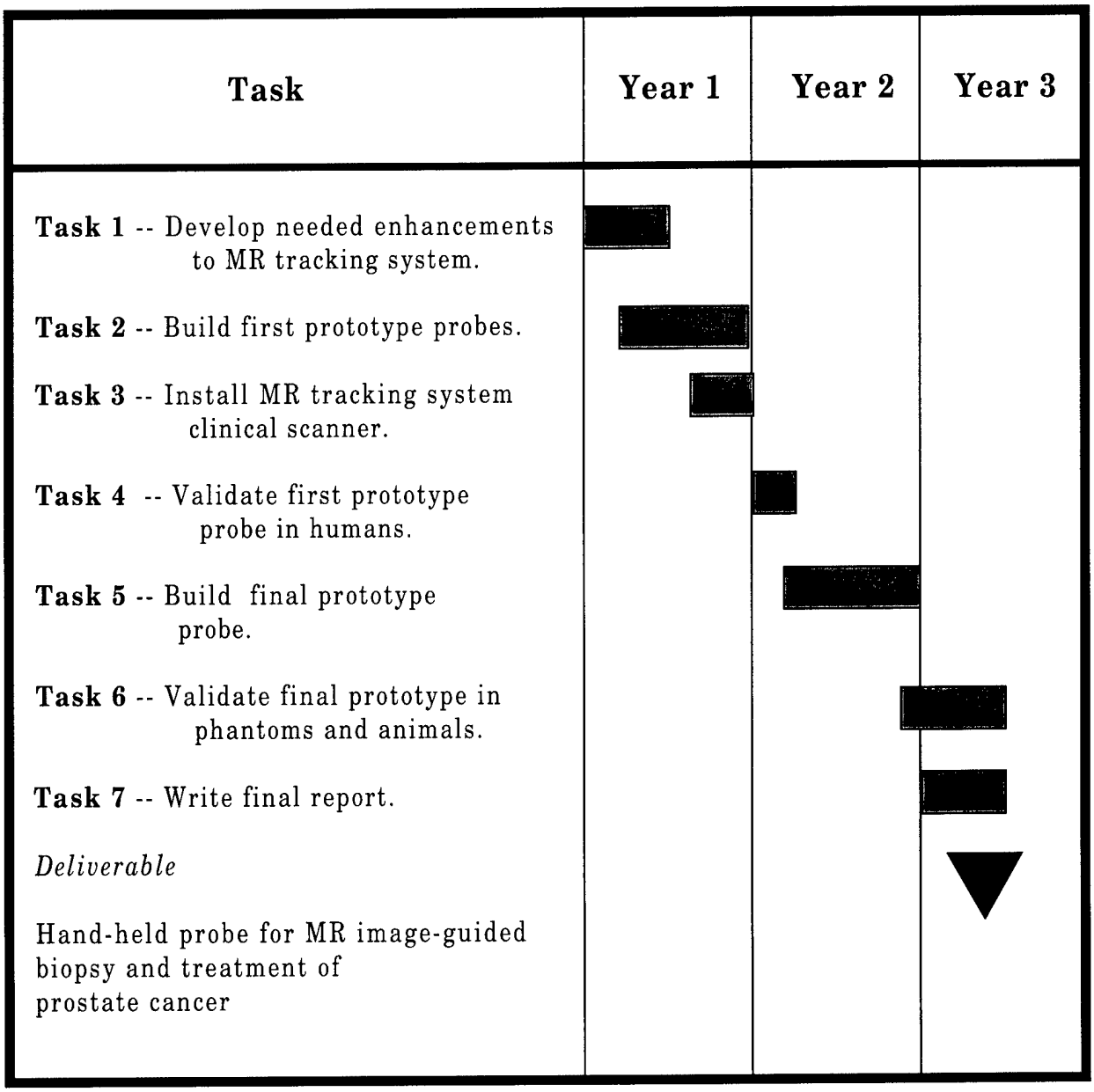


Figure 1. Schedule for the project as presented in the proposal. Note that Task 3 was eliminated in contract negotiations.

Table 1

Task 1. Develop needed enhancements to existing MR tracking system. Months 1-6.

- Incorporate parametric description of probe for enhanced visualization on display screen.
- Make pulse sequence improvements to optimize image contrast.
- Integrate surface coil imaging and tracking functions into tracking software system.

Task 2. Build first prototype probes (which include only imaging and tracking coils). Months 3-12

- Evaluate commercially available prostate imaging probes.
- Integrate three or more tracking coils into a prostate imaging probe, rebuild probe if necessary.

Task 3. Install MR tracking system on clinical scanner. Months 9-12

- Identify clinical partner.
- Acquire and construct MR tracking hardware.
- Install and validate MR tracking at clinical site.

Task 4. Validate first prototype probe in humans. Months 13-15

- Perform safety review.
- Apply for and receive IRB approval.
- Make images in six human volunteers.

Task 5. Build final prototype probes (which includes biopsy needle channels). Months 15-24

- Identify suitable MR compatible biopsy needle.
- Review design concepts with practicing clinicians.
- Design and construct MR guided biopsy probe.

Task 6. Validate final prototype in phantoms and animals. Months 24-30

- Validate biopsy needle placement in phantoms.
- Demonstrate prostate biopsy in animal model.

Task 7. Write final report. Months 27-30

- Write final report.
- Apply for phase 2 support.

Task 1 -- Develop needed enhancements to existing MR tracking system.

This task has three sub-tasks:

1. Incorporate parametric description of probe for enhanced visualization on display screen.
2. Make pulse sequence improvements to optimize image contrast.
3. Integrate surface coil imaging and tracking functions into tracking software system.

Sub-task 1

This sub-task is only partially complete. An algorithm that allows a non-parametric description of the device being tracked has been created. This algorithm allows the user to define the working coils to be part of a "group". Once defined, the relative distances between each coil are checked to validate the location of the device. No information regarding the geometry of the device is required.

Work has begun on the creation of a new "pop-up" menu that will allow the user to define and choose the device being tracked. Once a device is chosen, a graphic representation of the device will be displayed upon the acquired MR image in addition to the icons currently being displayed. Completion of this task is not essential to the completion of subsequent task. Nevertheless, completion is anticipated within the next few months.

Sub-task 2

This sub-task has been completed. The MR tracking pulse sequence now has the ability to acquire Gradient-echo, Spin-echo and Spiral images without re-downloading the scanner. Consequently, the user can rapidly switch between imaging modes as well as non-imaging modes such as tracking and profiling. Incorporation of Fast-Spin Echo imaging into the pulse sequence will be straightforward and is anticipated to be accomplished within the next year.

Sub-task 3

This sub-task has been completed. New capabilities have been added to the MR tracking software that permit the user to change the imaging parameters associated with all the imaging sequences. This was accomplished by creating a new "pop-up" menu that allows the user to define and/or recall an imaging protocol. A protocol includes the following information:

Scan type (e.g. Gradient-Echo, Spin-Echo, Fast-Spin Echo, etc.)
Signal source (normal imaging coil, tracking coil etc.)
Recon (scanner or workstation)
Scan parameters (TR, TE, FOV, NEX, Slice thickness, flip angle etc.)
Scan orientation (Axial, Sagittal, Coronal, Oblique etc.)

Changes to the pulse sequence software running on the MR scanner were also made to accommodate the new user interface.

Task 2 – Build first prototype probes

Both sub-tasks in this effort have been completed. Commercially available prostate probes from Med-Rad were acquired and evaluated. Several prototype probe designs, different from a standard trans-rectal ultrasound probe design, were conceived and built as "mock" probes. These prototype probes were tested in a cadaver model by Dr. Michael Moran, from St. Peter's Hospital, Albany NY. The prototype chosen for further development had superior properties in terms of access to the entire prostate and maneuverability in the rectum compared to the standard trans-rectal probe.

Line diagrams of the prototype prostate probe designed and built at GE's Research and Development Center are shown in Figures 2. Photographs of an actual probe are show in Figures 3a and 3b. The shell of the probe was designed on a computer and made using stereo lithography. The material used to construct the shell is an optically cured epoxy (SL-5190). The dimensions and shape of the probe were chosen in consultation with a practicing clinical urologist. We believe that this probe is the first to combine MR tracking, MR imaging and biopsy needle guidance for use in the prostate.

The probe contains an imaging coil with tuning and matching capacitors. The imaging coil is made of heavy gauge silver wire. Active de-tuning of the receive coil during transmission of an RF pulse is accomplished by forward biasing a decoupling diode. The probe also has three MR tracking coils embedded in its plane of symmetry (which also contains the needle track). The MR tracking coils are simple 10-turn solenoids wound around glass capillary tubes containing a solution of $CuSO_4$. Tuning and matching capacitors are not currently employed on the tracking coils. Sufficient room is available in the handle of the probe, however, to add tuning and matching capacitors and pre-amplifiers if needed.

The handle of the probe contains a channel for a biopsy needle. Although the probe is currently configured for manual insertion of the biopsy needle, a configuration incorporating a biopsy gun is being considered. The biopsy needle channel is positioned within the probe so that it is contained within the plane defined by the three tracking coils. Thus, when the scanner makes an image aligned with the tracking coils, the image also contains the needle path. Since the location of the needle channel is known with respect to the tracking coils, a graphical display of the needle trajectory can be superimposed upon the image prior to the actual insertion of the needle.

Figures 4a and 4b show high-resolution MR images made with the GE-built prostate probe and a probe made by Med-Rad (model number BPX-15). The Med-Rad probe has been approved by the FDA and is widely used for diagnostic prostate imaging. The images were acquired in a $CuSO_4$ bath under identical conditions. Both images were acquired with a 1.5 Tesla scanner. The system's body coil was used to excite the spin magnetization and

the probes were used for receiving the MR signals. A spin echo pulse sequence (TR= 500 ms, TE= 20 ms) with a 1.5 mm slice thickness and a 24 cm FOV was employed. The matrix size was 256x256 with a 16 kHz bandwidth.

Figure 5 shows the sensitivity profiles of the GE-built prostate probe and the Med-Rad probe. Note that even though the GE probe is physically smaller than the Med-Rad probe, the GE probe has greater sensitivity and depth of penetration. At a distance of 1 cm from the wall of the probe (i.e. approximately the distance to the prostate gland) the GE probe has more than twice the signal-to-noise ratio of the Med-Rad probe. This SNR advantage is maintained beyond a distance of 5 cm from the probe wall, a distance corresponding to the most distant part of the prostate gland.

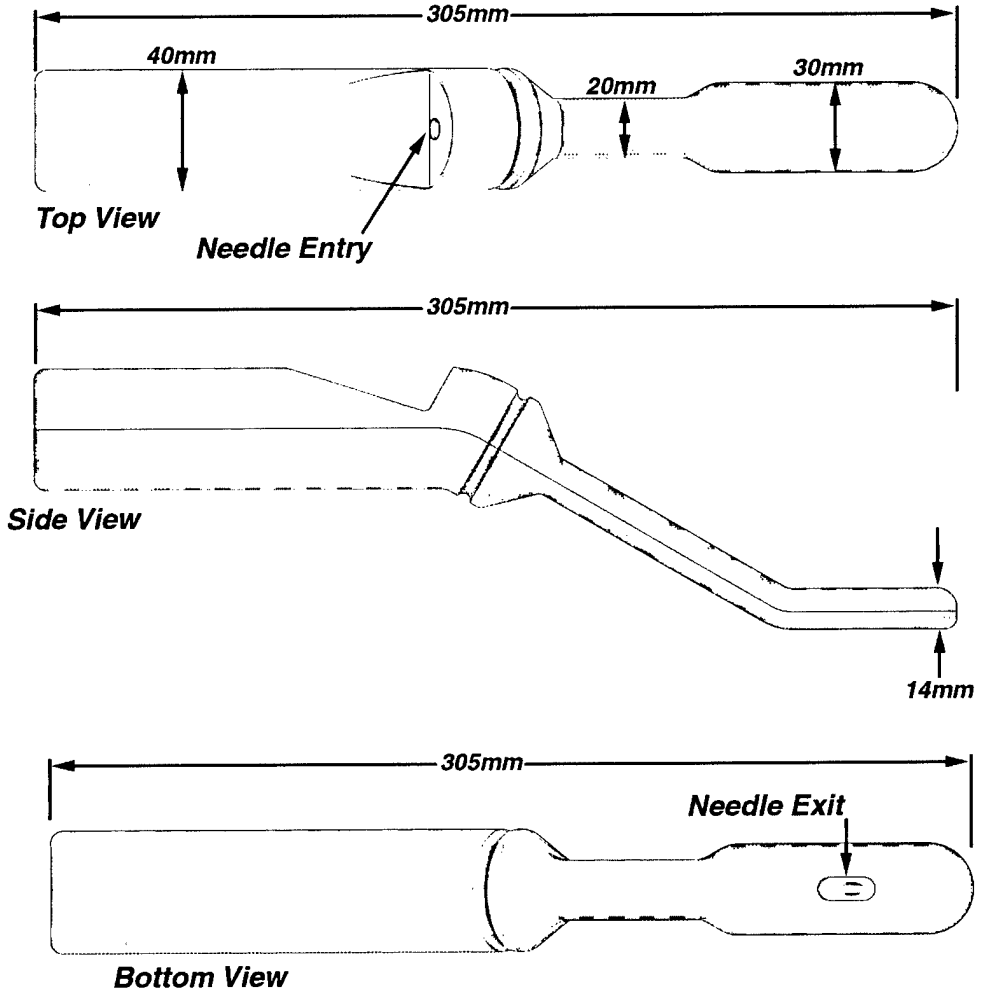


Figure 2. Top, side and bottom views of the MR image-guided biopsy probe for the prostate

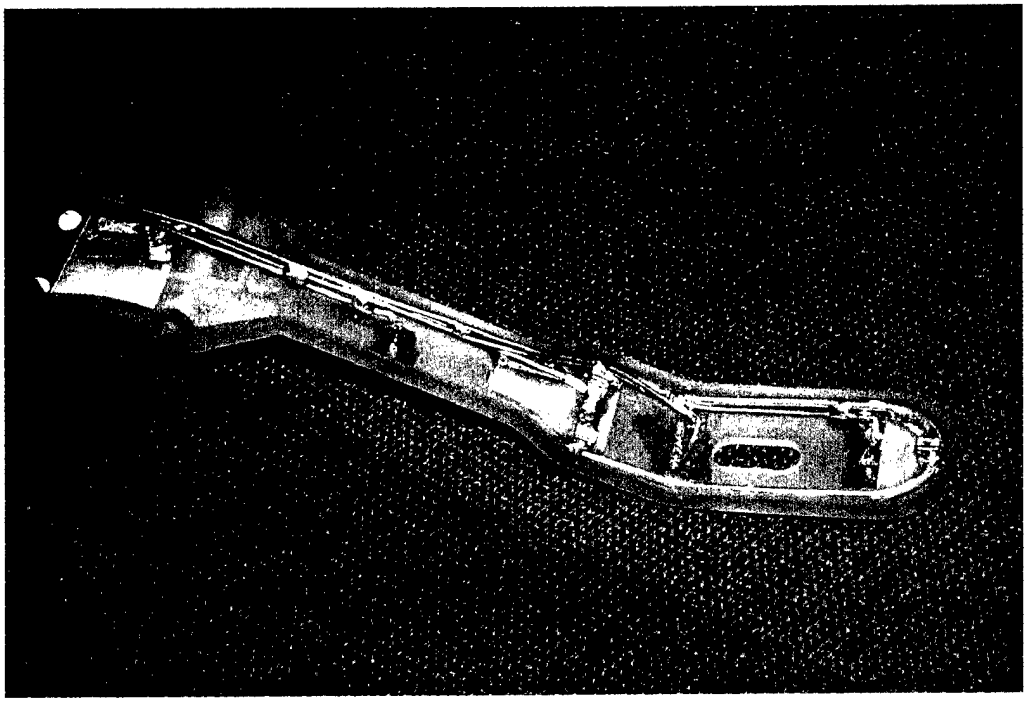


Figure 3a. Photograph of the prostate biopsy probe built at GE's Research and Development Center. The probe housing was made using stereo lithography and contains an imaging coil and three MR tracking coils. Note that in this photograph the top cover has been removed.

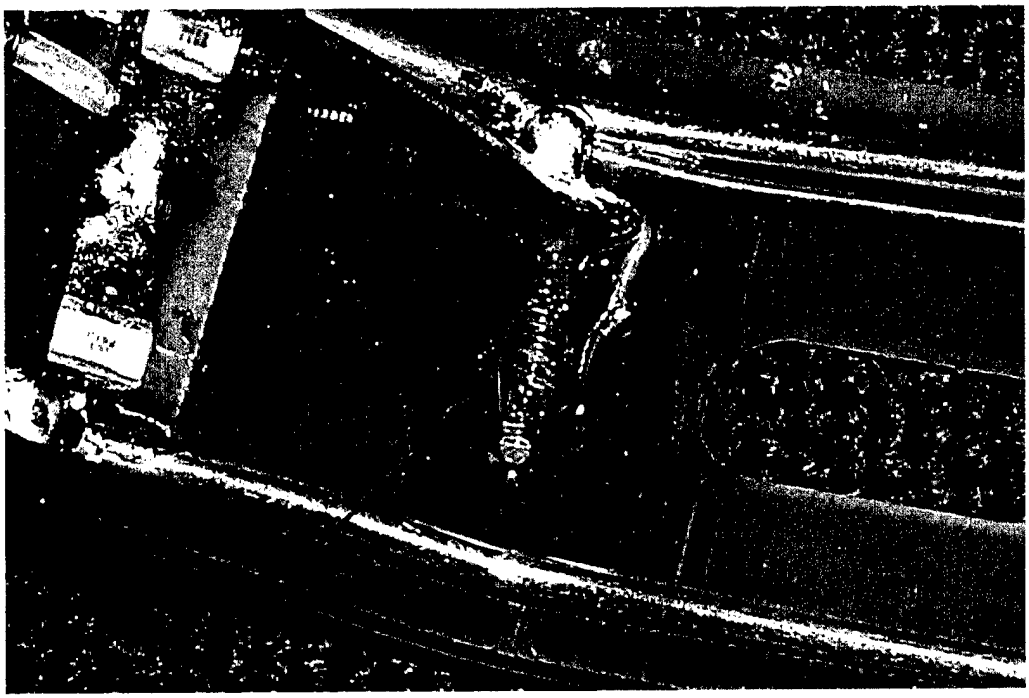
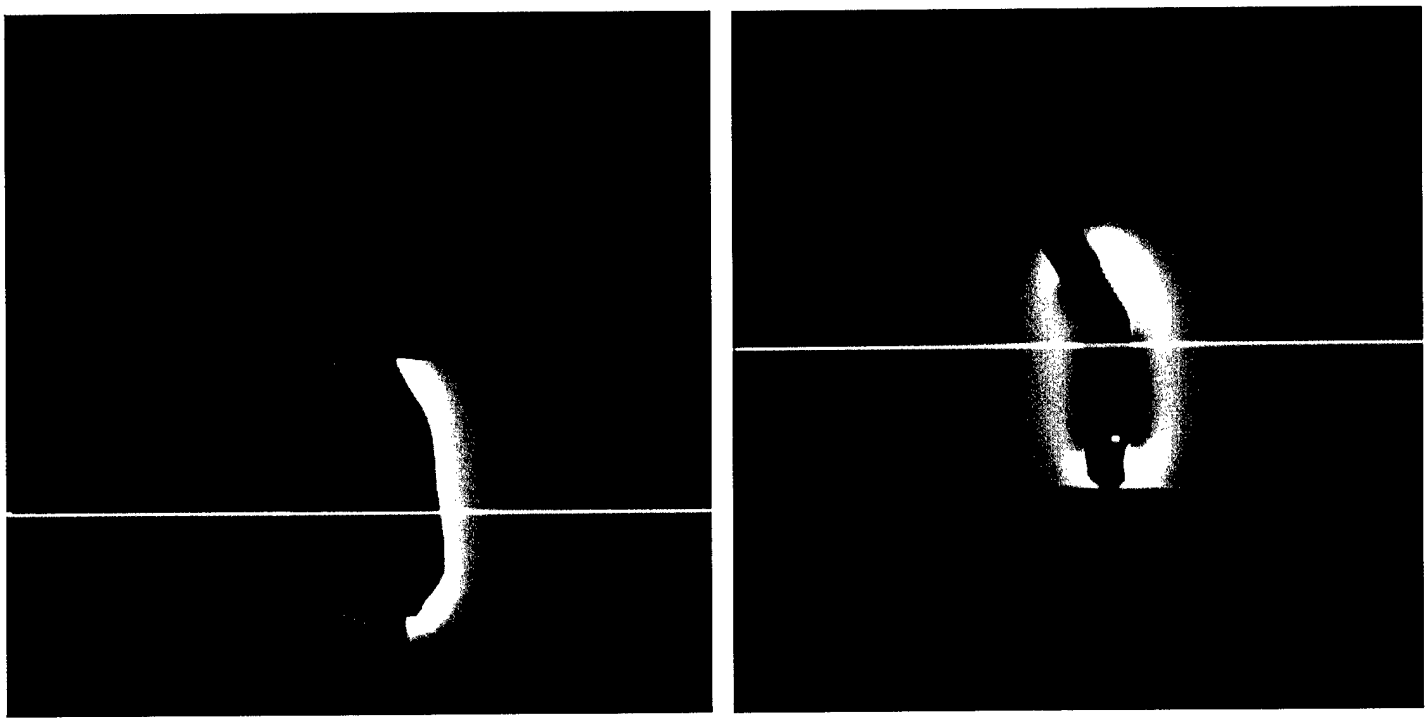


Figure 3b. Close-up photograph of one of the MR tracking coils contained within the prostate imaging probe.



A B

Figure 4. MR images acquired with A) a Med-Rad prostate probe and B) the GE-built probe. The horizontal line through each image indicates the region of the image analyzed in Figure 5.

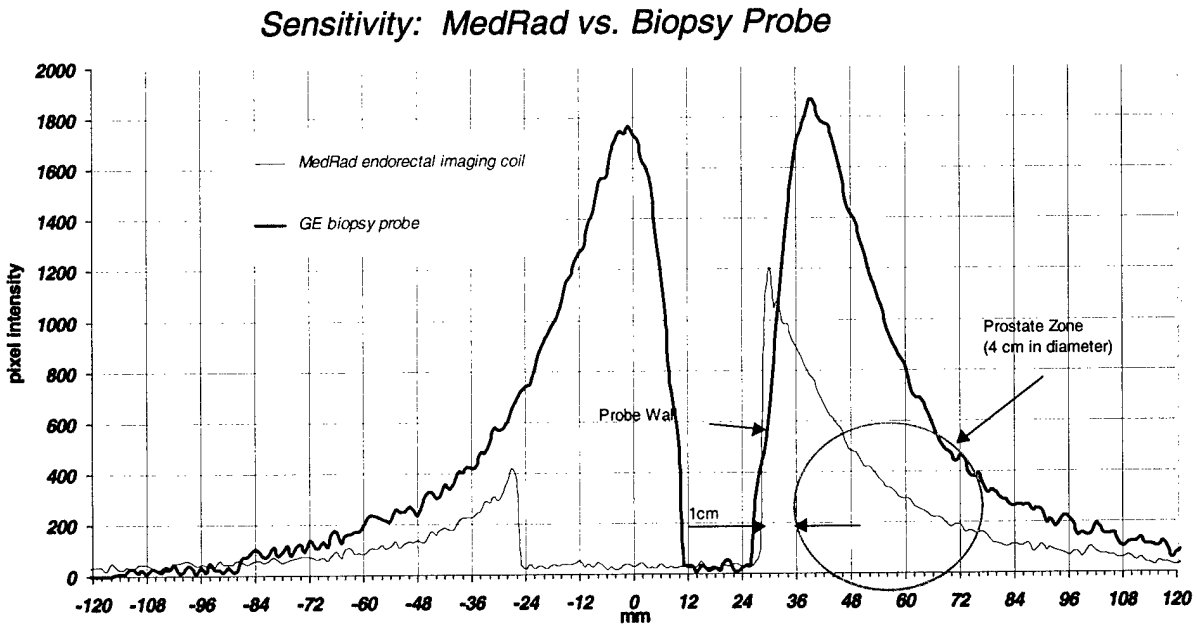


Figure 5. Intensity profiles showing sensitivity of the GE-built prostate coil and the Med-Rad coil.

Key Research Accomplishments

A. Enhancements made to the MR tracking system
   - Incorporation of non-parametric probe description complete
   - Incorporation of parametric probe description partially complete.
   - Pulse sequence enhancements made to optimize image contrast
      - Spin Echo
      - Gradient Echo
      - Spiral Imaging
   - Surface coil imaging and tracking functions integrated
      - "pop-up" menu to define imaging parameters created
      - pulse sequence changes made to interact with the new "pop-up" menu

B. First prototype probes built
   - Commercially available probe evaluated
   - Practicing clinical urologist consulted
   - A new probe design conceived and tested in a cadaver model
   - Prototype probe designed and built.
   - Imaging and tracking functions of prototype probe tested in phantoms
   - Prototype probe is smaller than commercially available probe, but has twice the Signal-to-Noise ratio at all depths of penetration.

Reportable Outcomes

1. An abstract for a presentation entitled: "Magnetic Resonance Tracking Image Guided Biopsy in Prostate", has been submitted to for presentation at the Eighth annual meeting of the International Society of Magnetic Resonance in Medicine (ISMRM). The authors are: R.D. Watkins, K.W. Rohling, E.E. Uzgiris, C.L. Dumoulin, R.D. Darrow and R.O. Giaquinto. Acknowledgment to the US Army is included.

2. A poster was presented by Dr. Michael Moran at the 17th World Congress on Endocrinology and SWL in Rhodes, Greece (September 2-5, 1999). The poster was entitled "Cadaveric Morphometrics for the use of a novel transrectal magnetic resonance (MR) image-guided focused ultrasonic ablation of the prostate". Authors of the poster were: AR Parekh, ME Moran, CJ Calvano, CL Dumoulin and EE Uzgiris. Acknowledgment to the US Army was included.

3. A disclosure letter entitled "A prostate Probe for MR image guided biopsy and MR guided delivery of therapy" was submitted to the General Electric Research and Development Center as the first step for filing a U.S. Patent. Inventors listed on the disclosure letter are: EE Uzgiris, KW Rohling, RD Watkins, RD Darrow and CL Dumoulin.

4. A proposal entitled "Hand-held probe for MR Image-Guided Focused Ultrasound treatment of Prostate Cancer" was submitted to the U.S. Army. This proposal received a score of 2.0 (excellent), but was not recommended for funding.

5. A joint proposal with the University of California at San Francisco (UCSF) entitled "Improved MRI/MRSI for biopsy guidance of prostate cancer" was submitted to the National Cancer Institute.

6. A proposal entitled "MR-guided focused ultrasound ablation of prostate cancer" was submitted to the National Cancer Institute.

Conclusions

In the first year of work on this project we have made enhancements to the MR tracking subsystem and we have constructed the first prototype probe for prostate imaging. The MR tracking enhancements permit greater flexibility in image acquisition and support new MR imaging schemes. Although parametric definition of a device within the MR tracking system is not yet fully supported, the software is now ready to be used for the remaining tasks of the project.

The prototype probe that we constructed incorporates three MR tracking coils and a sensitive MR imaging coil. Evaluation of this probe in phantoms shows that the probe should be capable of making images of the entire prostate with twice the signal-to-noise ratio (SNR) of the most widely used commercially available prostate imaging probe. We expect that this gain in SNR will be realized in humans and that the resulting improvement in image quality provided by the new MR probe will be medically significant, even if the probe used only for diagnostic imaging.

At this point the project is on schedule and all first year tasks have been completed with the exception of one minor sub-task. Execution of the first year's tasks have left us well positioned to perform the second year's tasks of a) demonstrating the probe in humans, and b) building a final prototype. No changes in the second year tasks are anticipated or requested.